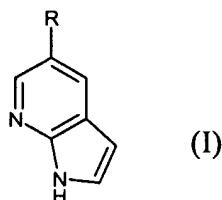


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of claims:

1. (Currently Amended) A compound of formula (I) as defined below:



wherein:

R stands for carbocyclyl, substituted carbocyclyl, ~~heterocyclyl, or substituted heterocyclyl~~, wherein

the optionally substituted carbocyclyl ~~or optionally substituted heterocyclyl~~ group is optionally fused to an unsaturated, partially unsaturated or fully saturated five to seven membered ring ~~containing zero to three heteroatoms~~,

each substitutable carbon atom in R, including the optional fused ring, is optionally and independently substituted by one or more of C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, carbocyclyl, or heterocyclyl, halogen, haloalkyl, OR<sup>2</sup>, SR<sup>2</sup>, NO<sub>2</sub>, CN, NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CONR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CO<sub>2</sub>R<sup>2</sup>, CO<sub>2</sub>R<sup>2</sup>, COR<sup>2</sup>, CONR<sup>2</sup>R<sup>2</sup>, S(O)<sub>2</sub>R<sup>2</sup>, SONH<sub>2</sub>, S(O)R<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>S(O)<sub>2</sub>R<sup>2</sup>, wherein each R<sup>2</sup> may be the same or different and is as defined below and wherein:

the C<sub>1-12</sub> alkyl optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R<sup>2</sup>)-, -S(O)- and -S(O<sub>2</sub>)- wherein each R<sup>2</sup> may be the same or different and is as defined below;

the C<sub>1-12</sub> alkyl, carbocyclyl, or heterocyclyl group is optionally substituted by one or more of halogen, haloalkyl, OR<sup>2</sup>, SR<sup>2</sup>, NO<sub>2</sub>, CN, NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CONR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CO<sub>2</sub>R<sup>2</sup>, CO<sub>2</sub>R<sup>2</sup>, COR<sup>2</sup>, CONR<sup>2</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>2</sup>, SONH<sub>2</sub>, S(O)R<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>S(O)<sub>2</sub>R<sup>2</sup>; wherein each R<sup>2</sup> may be the same or different and is as defined below and

the carbocyclyl, or heterocyclyl group is optionally substituted by one or more C<sub>1-12</sub> alkyl,

each saturated carbon in the optional fused ring is further optionally and independently substituted by =O, =S, =NNHR<sup>2</sup>, NNR<sup>2</sup>R<sup>2</sup>, =N-OR<sup>2</sup>, =NNHCOR<sup>2</sup>, =NNHCO<sub>2</sub>R<sup>2</sup>, =NNSO<sub>2</sub>R<sup>2</sup>, or =NR<sup>2</sup>, wherein each R<sup>2</sup> may be the same or different and is as defined below; and

each substitutable nitrogen atom in R is optionally substituted by R<sup>3</sup>, COR<sup>2</sup>, SO<sub>2</sub>R<sup>2</sup> or CO<sub>2</sub>R<sup>2</sup>, wherein each R<sup>2</sup> and R<sup>3</sup> may be the same or different and is as defined below;

R<sup>2</sup> is hydrogen, C<sub>1-12</sub> alkyl or aryl, optionally substituted by one or more of C<sub>1-4</sub> alkyl, halogen, C<sub>1-4</sub> haloalkyl, OR<sup>4</sup>, SR<sup>4</sup>, NO<sub>2</sub>, CN, NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CONR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CO<sub>2</sub>R<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, COR<sup>4</sup>, CONR<sup>4</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>4</sup>, SONH<sub>2</sub>, S(O)R<sup>4</sup>, SO<sub>2</sub> NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>S(O)<sub>2</sub>R<sup>4</sup>, wherein the C<sub>1-12</sub> alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R<sup>4</sup>)-, -S(O)- and -S(O<sub>2</sub>)-, wherein each R<sup>4</sup> may be the same or different and is as defined below;

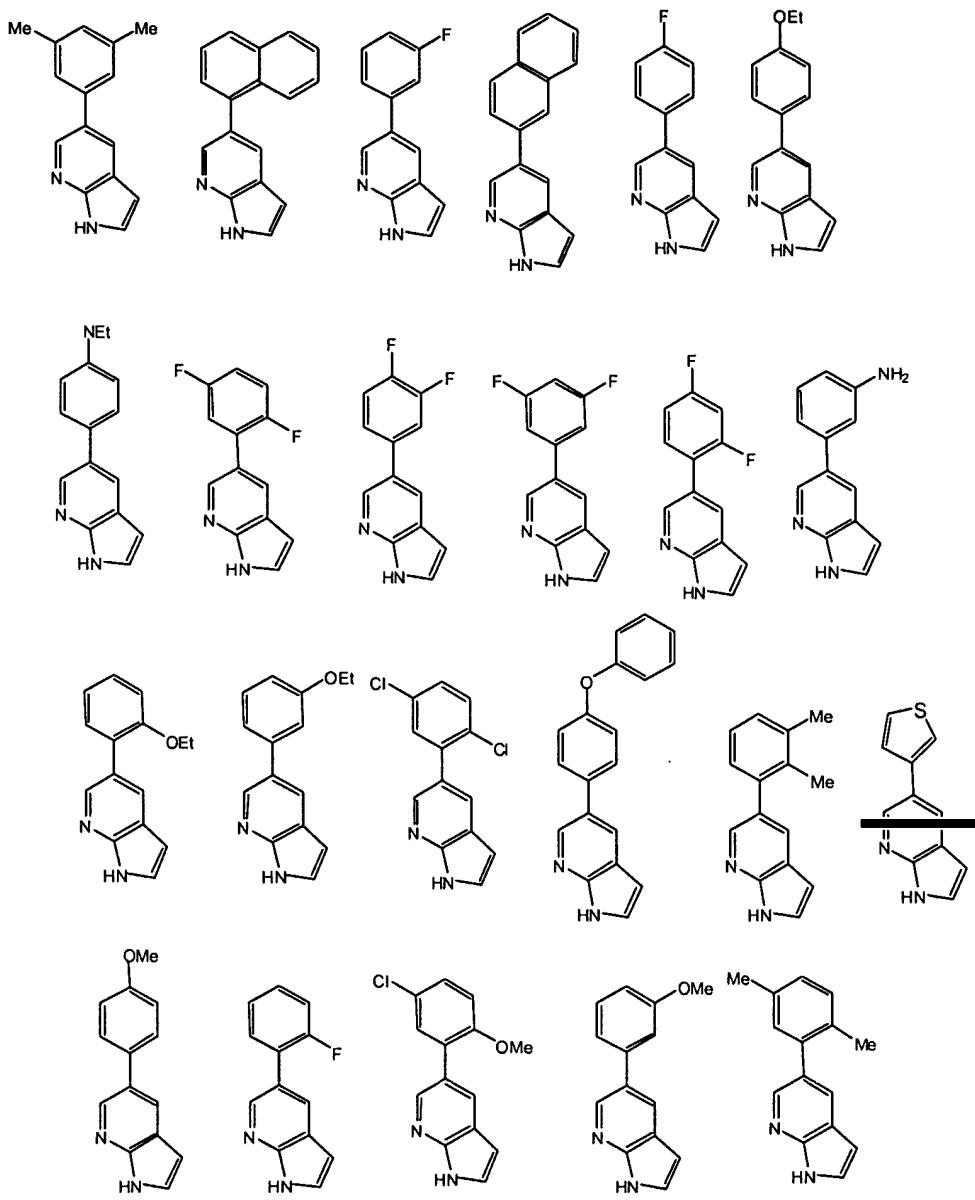
R<sup>3</sup> is C<sub>1-12</sub> alkyl or aryl, optionally substituted by one or more of C<sub>1-4</sub> alkyl, halogen, C<sub>1-4</sub> haloalkyl, OR<sup>4</sup>, SR<sup>4</sup>, NO<sub>2</sub>, CN, NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CONR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CO<sub>2</sub>R<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, COR<sup>4</sup>, CONR<sup>4</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>4</sup>, SONH<sub>2</sub>, S(O)R<sup>4</sup>, SO<sub>2</sub> NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>S(O)<sub>2</sub>R<sup>4</sup>, wherein the C<sub>1-12</sub> alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R<sup>4</sup>)-, -S(O)- and -S(O<sub>2</sub>)-, wherein each R<sup>4</sup> may be the same or different and is as defined below;

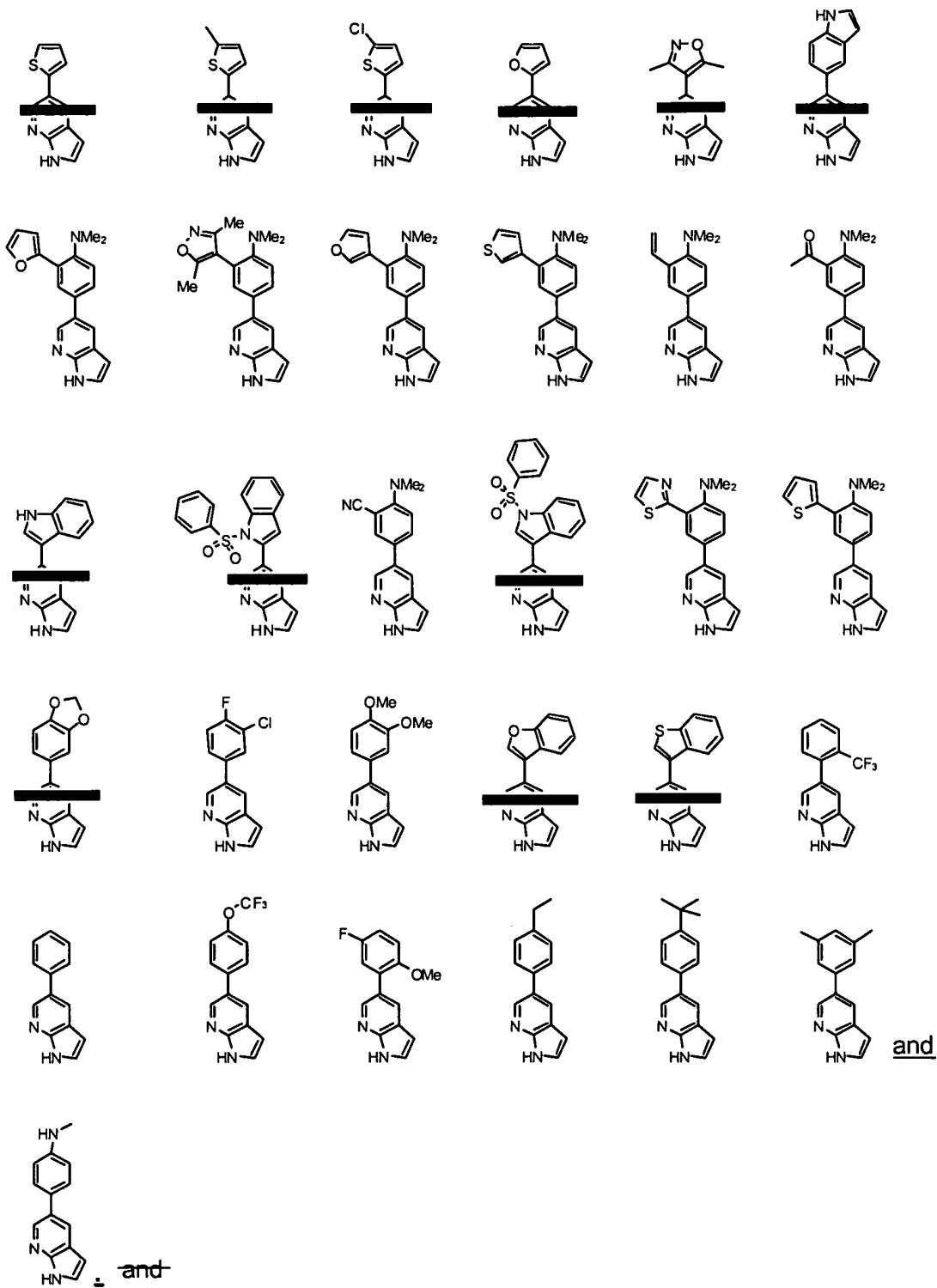
R<sup>4</sup> is hydrogen, C<sub>1-4</sub> alkyl, or C<sub>1-4</sub> haloalkyl; with the proviso that when R is phenyl substituted with branched C<sub>6</sub>-alkyl (-CH(CH<sub>2</sub>-CH(CH<sub>3</sub>)(CH<sub>3</sub>))-CH<sub>2</sub>-) incorporating two insertions -(CO)-and-NH-, the C<sub>6</sub>-alkyl group is not substituted with -CN;

and the pharmaceutically acceptable salts, ~~and other pharmaceutically acceptable biohydrolyzable derivatives thereof, selected from the group comprising esters, amides, carbamates, carbonates, ureides, solvates, hydrates, affinity reagents and prodrugs thereof.~~

2. (Currently Amended) A compound as claimed in claim 1, wherein R is an aryl or heteroaryl radical, optionally substituted with one or more of alkyl, haloalkyl, halogen, OR<sup>8</sup>, S R<sup>8</sup>, SO R<sup>8</sup>, (NR<sup>8</sup>)<sub>2</sub>, wherein R<sup>8</sup> is independently selected from hydrogen, C<sub>1-4</sub> alkyl or haloalkyl.

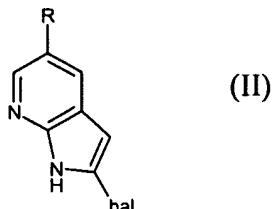
3. (Previously Presented) A compound as claimed in claim 1, wherein R is an optionally substituted aryl.
4. (Original) A compound as claimed in claim 3, wherein R is phenyl substituted in the 4-(para) position.
5. (Previously Presented) A compound as claimed in claim 4, wherein R is phenyl substituted by NR<sup>6</sup>R<sup>6</sup>; and wherein each R<sup>6</sup> is independently H or C<sub>1-4</sub> alkyl.
6. (Currently Amended) A compound as claimed in claim 3, wherein R is aryl substituted with is F, Cl, Br, or haloalkyl, or alkyl.
7. (Currently Amended) A compound as claimed in claim 1, wherein the compound is selected from the group consisting of:





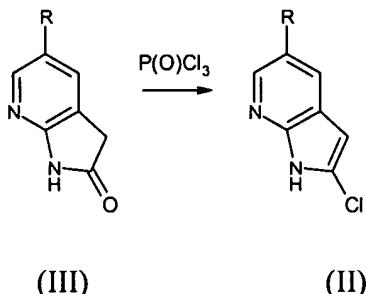
8. (Cancelled)

9. (Currently Amended) A process for the manufacture of the compounds of claim 1 which comprises hydrogenating a compound of the general formula (II):



wherein R is as defined in claim 1 and hal stands for a halogen atom, -C.

10. (Previously Presented) A process as claimed in claim 9, wherein the compound of the general formula (II) is made by halogenating a compound of the general formula (III) in the 2 position



where R is as defined above and hal stands for halogen.

11. (Original) A pharmaceutical formulation comprising a compound as defined in claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.

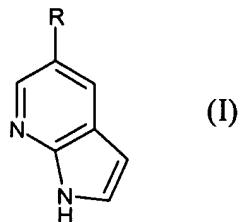
12. (Cancelled)

13. (Cancelled)

14. (Canceled)

15. (Canceled)

16. (Withdrawn) A method for inhibiting JNK the method comprising administering to a subject in need thereof a pharmaceutical formulation comprising a compound of formula (I)



wherein:

R stands for carbocyclyl, substituted carbocyclyl, heterocyclyl, or substituted heterocyclyl, wherein

the optionally substituted carbocyclyl or optionally substituted heterocyclyl group is optionally fused to an unsaturated, partially unsaturated or fully saturated five to seven membered ring containing zero to three heteroatoms,

each substitutable carbon atom in R, including the optional fused ring, is optionally and independently substituted by one or more of C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, carbocyclyl, or heterocyclyl, halogen, haloalkyl, OR<sup>2</sup>, SR<sup>2</sup>, NO<sub>2</sub>, CN, NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CONR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CO<sub>2</sub>R<sup>2</sup>, CO<sub>2</sub>R<sup>2</sup>, COR<sup>2</sup>, CONR<sup>2</sup>R<sup>2</sup>, S(O)<sub>2</sub>R<sup>2</sup>, SONH<sub>2</sub>, S(O)R<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>S(O)<sub>2</sub>R<sup>2</sup>, wherein each R<sup>2</sup> may be the same or different and is as defined below and wherein:

the C<sub>1-12</sub> alkyl optionally incorporates one or two insertions selected from the group consisting of -O-, -C(O)-, -N(R<sup>2</sup>)-, -S(O)- and -S(O<sub>2</sub>)- wherein each R<sup>2</sup> may be the same or different and is as defined below;

the C<sub>1-12</sub> alkyl, carbocyclyl, or heterocyclyl group is optionally substituted by one or more of halogen, haloalkyl, OR<sup>2</sup>, SR<sup>2</sup>, NO<sub>2</sub>, CN, NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CONR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>COR<sup>2</sup>, NR<sup>2</sup>CO<sub>2</sub>R<sup>2</sup>, CO<sub>2</sub>R<sup>2</sup>, COR<sup>2</sup>, CONR<sup>2</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>2</sup>, SONH<sub>2</sub>, S(O)R<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2</sup>, NR<sup>2</sup>S(O)<sub>2</sub>R<sup>2</sup>; wherein each R<sup>2</sup> may be the same or different and is as defined below and

the carbocyclyl, or heterocyclyl group is optionally substituted by one or more C<sub>1-12</sub> alkyl,

each saturated carbon in the optional fused ring is further optionally and independently substituted by =O, =S, =NNHR<sup>2</sup>, NNR<sup>2</sup>R<sup>2</sup>, =N-OR<sup>2</sup>, =NNHCOR<sup>2</sup>, =NNHCO<sub>2</sub>R<sup>2</sup>, =NNSO<sub>2</sub>R<sup>2</sup>, or =NR<sup>2</sup>, wherein each R<sup>2</sup> may be the same or different and is as defined below; and

each substitutable nitrogen atom in R is optionally substituted by R<sup>3</sup>, COR<sup>2</sup>, SO<sub>2</sub>R<sup>2</sup> or CO<sub>2</sub>R<sup>2</sup>, wherein each R<sup>2</sup> and R<sup>3</sup> may be the same or different and is as defined below;

R<sup>2</sup> is hydrogen, C<sub>1-12</sub> alkyl or aryl, optionally substituted by one or more of C<sub>1-4</sub> alkyl, halogen, C<sub>1-4</sub> haloalkyl, OR<sup>4</sup>, SR<sup>4</sup>, NO<sub>2</sub>, CN, NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CONR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CO<sub>2</sub>R<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, COR<sup>4</sup>, CONR<sup>4</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>4</sup>, SONH<sub>2</sub>, S(O)R<sup>4</sup>, SO<sub>2</sub> NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>S(O)<sub>2</sub>R<sup>4</sup>, wherein the C<sub>1-12</sub> alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R<sup>4</sup>)-, -S(O)- and -S(O<sub>2</sub>)-, wherein each R<sup>4</sup> may be the same or different and is as defined below;

R<sup>3</sup> is C<sub>1-12</sub> alkyl or aryl, optionally substituted by one or more of C<sub>1-4</sub> alkyl, halogen, C<sub>1-4</sub> haloalkyl, OR<sup>4</sup>, SR<sup>4</sup>, NO<sub>2</sub>, CN, NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CONR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>COR<sup>4</sup>, NR<sup>4</sup>CO<sub>2</sub>R<sup>4</sup>, CO<sub>2</sub>R<sup>4</sup>, COR<sup>4</sup>, CONR<sup>4</sup><sub>2</sub>, S(O)<sub>2</sub>R<sup>4</sup>, SONH<sub>2</sub>, S(O)R<sup>4</sup>, SO<sub>2</sub> NR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>S(O)<sub>2</sub>R<sup>4</sup>, wherein the C<sub>1-12</sub> alkyl group optionally incorporates one or two insertions selected from the group consisting of -O-, -N(R<sup>4</sup>)-, -S(O)- and -S(O<sub>2</sub>)-, wherein each R<sup>4</sup> may be the same or different and is as defined below;

R<sup>4</sup> is hydrogen, C<sub>1-4</sub> alkyl, or C<sub>1-4</sub> haloalkyl;

and the pharmaceutically acceptable salts, and other pharmaceutically acceptable biohydrolyzable derivatives thereof, selected from the group comprising esters, amides, carbamates, carbonates, ureides, solvates, hydrates, affinity reagents and prodrugs thereof.

17. (Withdrawn) The method of claim 16, wherein JNK is JNK3.

18. (Withdrawn) A method for the prevention or treatment of a JNK-mediated disorder, the method comprising administering to a subject in need thereof the pharmaceutical formulation of claim 11.

19. (Withdrawn) The method of claim 18, wherein the disorder is a neurodegenerative disorder, an inflammatory disease, a disorder linked to apoptosis, neuronal apoptosis, an autoimmune disease, destructive bone disorder, proliferative disorder, cancer, infectious disease, allergy, ischemia reperfusion injury, heart attack, angiogenic disorder, organ hypoxia, vascular hyperplasia, cardiac hypertrophy, thrombin induced platelet aggregation and/or a condition associated with prostaglandin endoperoxidase synthase-2.

20. (Withdrawn) The method of claim 19, wherein the neurodegenerative disorder is linked to apoptosis and/or is an inflammatory disease.

21. (Withdrawn) The method of claim 18, wherein the neurodegenerative disorder is: dementia; Alzheimer's disease; Parkinson's disease; Amyotrophic Lateral Sclerosis; Huntington's disease; senile chorea; Sydenham's chorea; hypoglycemia; head and spinal cord trauma, traumatic head injury; acute pain, chronic pain; epilepsy, seizures; olivopontocerebellar dementia; neuronal cell death; hypoxia-related neurodegeneration; acute hypoxia; glutamate toxicity, glutamate neurotoxicity; cerebral ischemia; dementia linked to meningitis, and/or dementia linked to neurosis; cerebrovascular dementia; or dementia in an HIV-infected patient.

22. (Withdrawn) The method of claim 18, wherein the neurodegenerative disorder is a peripheral neuropathy, mononeuropathy, multiple mononeuropathy, polyneuropathy, Lyme disease, or uremia; peripheral neuropathy caused by a toxic agent; a demyelinating disease, acute inflammatory polyneuropathy, chronic inflammatory polyneuropathy, leukodystrophies, Guillain-Barré syndrome; multiple mononeuropathy secondary to a collagen vascular disorder; multiple mononeuropathy secondary to sarcoidosis; multiple mononeuropathy secondary to a metabolic disease; or multiple mononeuropathy secondary to an infectious disease.

23. (Withdrawn) The method of claim 18, wherein the disorder is inflammatory bowel disorder; bronchitis; asthma; acute pancreatitis; chronic pancreatitis; allergies of; Alzheimer's disease; autoimmune disease, rheumatoid arthritis, systemic lupus erythematosus, glomerulonephritis, scleroderma, chronic thyroiditis, Graves's disease, autoimmune gastritis,

diabetes, autoimmune haemolytic anaemia, autoimmune neutropaenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, ulcerative colitis, Crohn's disease, psoriasis, or graft vs host disease.

24. (Canceled)

25. (Canceled)

26. (Canceled)

27. (Canceled)

28. (Canceled)

29. (Canceled)

30. (Canceled)

31. (Withdrawn) A method as claimed in claim 18, wherein one or more other active agent is administered to the individual simultaneously, subsequently, or sequentially to administering the compound.

32. (Withdrawn) A method as claimed in claim 31, wherein the other active agent is an anti-inflammatory agent such as a p38 inhibitor.

33. (Canceled)

34. (Canceled)

35. (Canceled)

36. (Canceled)

37. (Canceled)

38. (Canceled)

39. (Canceled)

40. (Canceled)

41. (Withdrawn) An assay for determining the activity of the compounds as defined in claim 1, comprising providing a system for assaying the activity and assaying the activity of a compound as defined in claim 1.

42. (Withdrawn) An assay as claimed in claim 41, wherein the assay is for the JNK inhibiting activity of the compound.

43. (Withdrawn) An assay as claimed in claim 41, wherein the assay is a Scintillation Proximity Assay (SPA) using radiolabelled ATP, or is ELISA.

44. (Canceled)

45. (Withdrawn) A method as claimed in claim 44, which is performed in a research model.

46. (Withdrawn) A method as claimed in claim 45, wherein the research model is an animal model.

47. (Previously Presented) The compound of claim 3, wherein R is selected from the group consisting of phenyl and naphthyl.

48. (Previously Presented) The compound of claim 6, wherein R is aryl substituted with fluorine.

49. (Previously Presented) The compound of claim 6, wherein the haloalkyl is CF<sub>3</sub>.
50. (Previously Presented) The compound of claim 6, wherein the alkyl is selected from the group consisting of methyl, ethyl, and propyl.
51. (Cancelled)
52. (Withdrawn) The assay of claim 41, wherein the assay is for the JNK3 specific inhibiting activity of the compound.